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10/596,516	12/16/2008	Walter Keith Jones	91830.0542770	7508

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,516	JONES, WALTER KEITH	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1,3 and 8-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application 10/596,516 is a 371 of PCT/US2004/042950 filed on 12/20/2004 which claims benefit of 60/531,399 filed on 12/19/2003 and claims benefit of 60/574,131 filed on 05/25/2004.

Election/Restriction

Applicant's election without traverse of Group II, claim 2, drawn to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule comprising at least two end-to-end repeated copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys, in the reply filed on 10/12/2010 is acknowledged.

Claim 18 is cancelled. Claims 2-12, 14-17, and 27-29 are amended. It is noted that claims 4-7 have been amended to be dependent claims of claim 2, instead of being dependent claims of claim 1. Accordingly, claims 4-7 are re-assigned to be claims of Group II invention.

Claims 1-17 and 19-29 are pending in the instant application.

Claims 1, 3, 8-17, and 19-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 2 and 4-7 are currently under examination.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 2 and 4-7 are rejected under 35 U.S.C. 102(a) and under 102(e) as being anticipated by **Dzau et al.** (US 2003/0186922, publication date 10/02/2003, filed on 04/25/2003, priority date 10/29/1993).

Claim 2 is directed to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule comprising at least two end-to-end repeated copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys.

Claim 4 is directed to the transcription factor decoy of claim 1, further comprising at least one tissue-specific promoter.

Claim 5 is directed to the transcription factor decoy of claim 1, wherein the decoy is capable of blocking signaling and gene expression associated with pathogenesis.

Claim 6 is directed o the transcription factor decoy of claim 1, wherein the decoys are NF-κB-specific.

Claim 7 is directed to the transcription factor decoy of claim 1, wherein the transcription factor is selected from NF-κB, AP-1, ATF2, ATF3, and SP1.

Claim interpretations: The limitation "tissue-specific promoter" recited in claim 4 is interpreted as any promoter that is not ubiquitously and constitutively active in all tissues.

With regard to the limitation of claims 2 and 5, **Dzau et al.** teach oligodeoxynucleotide decoys for the prophylactic or therapeutic treatment of diseases associated with the binding of endogenous transcription factors to genes involved in cell growth, differentiation and signaling

or to viral genes. By inhibiting endogenous trans-activating factors from binding transcription regulatory regions, the decoys modulate gene expression and thereby regulating pathological processes including inflammation, intimal hyperplasia, angiogenesis, neoplasia, immune responses and viral infection (See abstract, Dzau et al., 2003).

Dzau et al., teaches double-stranded DNA molecule comprising complementary decoy oligonucleotides containing two E2F transcription factor binding sites:

decoys-2: 5'-GATCAAAGAACTGAATCAAAGAACTGAATC-3'
3'-CTAGTTT CTTGACTTAGTTT CTTGA CTTAG-5'

(See paragraph [0038], Dzau et al., 2003).

With regard to the limitation of claim 4, Dzau et al., teaches the decoys may comprise a portion of a larger plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence. Plasmids comprising promoter that regulates the expresses transcription factor decoy of interest are selected based on *compatibility with the target cell* (i.e. tissue specificity), size and restriction sites, replicative frequency, copy number maintenance, etc. For example, plasmids with relatively short half-lives in the target cell are preferred in situations where it is desirable to maintain therapeutic transcriptional modulation for less than the lifetime of the target cell (See paragraph [0021], Dzau et al., 2003).

With regard to the limitation of claims 6 and 7, Dzau et al., teaches dsDNA is characterized by having a sequence specific for binding to a transcription factor, wherein said transcription product of said gene is necessary for cell proliferation, herein said transcription factor is E2F, AP-1 or NF-κB (See paragraph [0017], Table 1 on page 2, and claims 9 and 11, Dzau et al., 2003).

Thus, Dzau et al. clearly anticipates claims 2 and 4-7 of instant application.

2. Claims 2, 4, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992).

Claim 2 is directed to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule comprising at least two end-to-end repeated copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys.

Claim 4 is directed to the transcription factor decoy of claim 1, further comprising at least one tissue-specific promoter.

Claim 5 is directed to the transcription factor decoy of claim 1, wherein the decoy is capable of blocking signaling and gene expression associated with pathogenesis.

Claim 7 is directed to the transcription factor decoy of claim 1, wherein the transcription factor is selected from NF-κB, AP-1, ATF2, ATF3, and SP1.

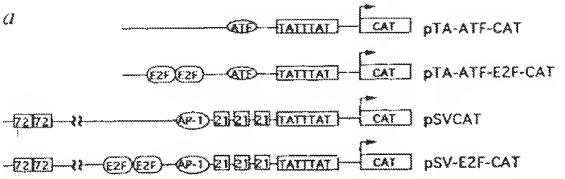
Claim interpretations: The limitation "tissue-specific promoter" recited in claim 4 is interpreted as any promoter that is not ubiquitously and constitutively active in all tissues.

With regard to the limitation of transcription factor decoy recited in claim 2 and the limitation regarding gene expression associated with pathogenesis recited in claim 5, **Weintraub et al.** teaches that originally E2F sites were identified as elements in the promoters of adenovirus early genes that are necessary for activation of these genes by the early protein E1a (ref. 1). E2F promoter elements have been shown to be important for transcriptional activation of several genes critical for progression through the cell cycle. Weintraub et al. teaches that during the G1 phase of the cell cycle, the E2F protein forms a complex with the cell-cycle protein Rb (retinoblastoma) and it has been suggested that this binding of Rb to E2F inactivates E2F.

Weintraub et al. shows that Rb-E2F is an active complex that, when bound to the E2F site, inhibits the activity of other promoter elements and thus silences transcription. Weintraub et al. proposes that the ability of this complex to inhibit transcription is integral to the function of Rb and provide evidence that E2F is a positive element in the absence of an active form of Rb. Weintraub et al. teaches that binding of Rb to E2F depends on the phosphorylation state of Rb (only the under-phosphorylated form binds) and that the phosphorylation state of Rb changes during progression through the cell cycle. Weintraub et al. suggest that the E2F site alternates between a positive and negative element with the phosphorylation/dephosphorylation cycle of Rb, and this cyclic activity may be responsible for activating and then inhibiting genes during the cell cycle (See abstract, Weintraub et al., 1992).

With regard to the characteristics regarding transcription factor decoy recited in claims 2, 4, 5, and 7, Weintraub et al. teaches that the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*). This competitive binds and sequesters E2F, thus preventing it from interacting with the *E1a* promoter (See left column, page 259, Weintraub et al., 1992).

The diagram of the plasmids taught by Weintraub et al. in Figure 2a is shown below.



It is noted that there are multiple end-to-end E2F sites present in the promoter of double-stranded plasmid pTA-ATF-E2F-CAT and plasmid pSV-E2F-CAT. Furthermore, the AP-1 site and ATF site present in the plasmids taught by Weintraub et al. are the binding sites of transcription factors AP-1, ATF2 and ATF3 recited in claim 7 of instant application.

Thus, Weintraub et al. clearly anticipates claims 2, 4, 5, and 7 of instant application.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 2 and 6 are ejected under 35 U.S.C. 103(a) as being unpatentable over **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992) in view of **Sharma et al.** (Sharma et al.

Transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis, *Anticancer Research*, 16(1): 61-69, 1996)

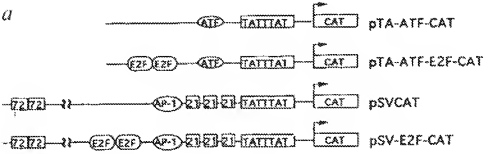
Claim 2 is directed to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule comprising at least two end-to-end repeated copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys

Claim 6 is directed o the transcription factor decoy of claim 1, wherein the decoys are NF-κB-specific.

Weintraub et al. teaches that originally E2F sites were identified as elements in the promoters of adenovirus early genes that are necessary for activation of these genes by the early protein E1a (ref. 1). E2F promoter elements have been shown to be important for transcriptional activation of several genes critical for progression through the cell cycle. Weintraub et al. teaches that during the G1 phase of the cell cycle, the E2F protein forms a complex with the cell-cycle protein Rb (retinoblastoma) and it has been suggested that this binding of Rb to E2F inactivates E2F. Weintraub et al. shows that Rb-E2F is an active complex that, when bound to the E2F site, inhibits the activity of other promoter elements and thus silences transcription. Weintraub et al. proposes that the ability of this complex to inhibit transcription is integral to the function of Rb and provide evidence that E2F is a positive element in the absence of an active form of Rb. Weintraub et al. teaches that binding of Rb to E2F depends on the phosphorylation state of Rb (only the under-phosphorylated form binds) and that the phosphorylation state of Rb changes during progression through the cell cycle. Weintraub et al. suggest that the E2F site alternates between a positive and negative element with the phosphorylation/dephosphorylation cycle of Rb, and this cyclic activity may be responsible for activating and then inhibiting genes during the cell cycle (See abstract, Weintraub et al., 1992).

With regard to the transcription factor decoy recited in claim 2, Weintraub et al. teaches that the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*). This competitive binds and sequesters E2F, thus preventing it from interacting with the *E1a* promoter (See left column, page 259, Weintraub et al., 1992).

The diagram of the plasmids taught by Weintraub et al. in Figure 2a is shown below.



It is noted that there are multiple end-to-end E2F sites present in the promoter of double-stranded plasmid pTA-ATF-E2F-CAT and plasmid pSV-E2F-CAT.

Weintraub et al. (1992) does not explicitly teach the limitation "wherein the decoys are NF-κB-specific" recited in claim 6 of instant application.

At the time the claimed invention was made, transfection factor decoy for NF-kappaB transcription factor were known in the art. For instance, **Sharma et al.** (1996) teaches transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis. In an effort to decipher the role of homo- vs heterodimeric NNF-kappa B in regulating tumor cell growth, Sharma et al. used a decoy approach to trap these complexes in vivo. Using double-stranded phosphorothioates as a direct in vivo competitor for homo- vs heterodimeric NF-kappa

B, Sharma et al. demonstrate that decoys more specific to RelA inhibit growth tumor cell growth in vitro. Sharma et al. demonstrate that RelA, either as a homodimer or a heterodimer with some other members of the Rel family and not the classical NF-κB (RelA/NFKB1), is involved in the differential growth control of tumor cells (See abstract, Sharma et al., 1996).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Weintraub et al. regarding transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule comprising at least two end-to-end repeated copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys, with the teachings of Sharma et al. regarding transcription factor decoy approach to decipher the role of NF-κB transcription factor in oncogenesis, to arrive at claimed methods recited in claim 6 of instant application, by replacing E2F transcription factor binding sites taught by Weintraub et al. with NF-κB transcription factor binding sites taught by Sharma et al.

One having ordinary skill in the art would have been motivated to combine the teachings of Weintraub et al. with the teachings of Sharma et al. because Sharma et al. specifically teach a functional role of NF-κB transcription factor in regulation of oncogenesis whereas Weintraub et al. teaches retinoblastoma (RB) protein regulating E2F transcription factor binding to E2F sites.

There would have been a reasonable expectation of success given (i) the successful demonstration of plasmids with multiple E2F transcription factor binding sites functioning as a transcription factor decoy that sequesters E2F transcription factor and thus preventing E2F transcription factor from interacting with the *E1a* promoter, by the teachings of Weintraub et al., and (ii) the successful demonstration of transcription factor decoy approach to decipher the role

of homo- vs heterodimeric NNF-κB in regulating tumor cell growth, by the teachings of Sharma et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

4. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Primary Examiner
Art Unit 1632